1086-155 Ventilatory Response to Exercise Improves Risk Stratification in Chronic Heart Failure Patients With Intermediate Functional Capacity

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Background: Peak oxygen consumption (pVO2) has a relevant prognostic role in chronic heart failure (CHF), but its discriminatory power is limited in patients (pts) with intermediate exercise capacity (pVO2 between 10-18 ml/kg/min.), thus, supplementary exertional indexes are most needed. Methods: Six hundred CHF pts with left ventricular ejection fraction (LVEF) <=40% who performed a symptom-limited cardiopulmonary exercise testing were followed up for 780±450 days. Results: Eighty-seven pts had major cardiac events (77 cardiac deaths and 10 urgent heart transplantations). Multivariate analysis revealed the rate of increase of minute ventilation per unit of increase of carbon dioxide production (VE/VCO2 slope) (chi2, 79.3, p<0.0001), LVEF (chi2, 24.6, p<0.0001) and pVO2 (chi2, 9,4, p<0.0001), as independent and additional predictors of major cardiac events. Cardiac events were significantly different in pts with pVO2 lower or equal to10 ml/kg/min. compared to those with pVO2 greater or equal to 18 ml/kg/min.(37% vs 2% p<0.0001), whereas no difference was found among 403 pts with intermediate exercise capacity (17% in those with pVO2 greater than 10 to lower or equal to 14 ml/kg/min vs 11% in those with pVO2 greater than 14 to lower than 18 ml/kg/min). In this cohort, VE/CO2 slope resulted the strongest independent predictor of major cardiac events (chi2, 20.9, p=0.0001) at multivariate analysis adjusted for NYHA functional class, LVEF, peak systolic blood pressure, percentage of predicted VO2, VO2 at ventilatory anaerobic threshold (VAT), and detectable VAT. The best cut off value for VE/VCO2 slope was 35 (chi2, 25.8; RR= 3.2, 95% CI 2.0-5.1, p<0.0001): total mortality rate was 10% in pts with VE/VCO2 slope lower than 35 (n= 300: 74%) and 30% in those with VE/VCO2 slope greater or equal to 35 (n=103: 26%) (p<0.0001) and these pts showed comparable total mortality rate than those with pVO2 lower or equal to 10 ml/kg/min. (30% vs 37%: NS). Conclusions. A rational and pragmatic risk stratification process should involve both pVO2 and VE/VCO2 slope, distinctively, in patients with intermediate exercise capacity, as it offers an efficient predictive contribution for almost one fourth of them.

1086-156 The Effect of Angiotensin-Converting Enzyme Inhibitor on Exercise Tolerance Time in Patients With Left Ventricular Dysfunction

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Background: Despite controversy, the predominant concept states that angiotensin-converting enzyme (ACE) inhibitors improve exercise tolerance in patients with congestive heart failure. This study was therefore performed to evaluate whether an ACE inhibitor (trandolapril) prolongs exercise tolerance time in patients with left ventricular dysfunction after myocardial infarction.

Methods: In a prospective sub-study within Trandolapril Cardiac Evaluation study (TRACE), 305 patients (150 on placebo and 155 on trandolapril) with left ventricular dysfunction after myocardial infarction, were enrolled into a series of bicycle ergometry exercise tests at 1, 3, and 12 months. Exercise time was measured in every test.

Results: The two treatment groups were well matched at the baseline. The majority of the patients were in NYHA classes II and I. Exercise tolerance time increased in both placebo and trandolapril groups from 8.3±3.6 versus 8.7±3.5 minutes respectively at baseline to 9.0±3.7 versus 9.1±3.6 minutes respectively after three months, and to 9.7±3.8 versus 9.8±3.5 minutes respectively after 12 months. These changes were insignificant when compared the two treatment groups (P-values > 0.05).

Conclusions: Trandolapril does not improve exercise tolerance time in patients with left ventricular dysfunction after myocardial infarction. In contrast to the current concept, the TRACE study failed to confirm that ACE inhibitors have any effect on exercise tolerance.

1086-157 Lean Tissue-Adjusted Versus Body Weight-Adjusted Peak Oxygen Consumption and Mortality Prediction in Chronic Heart Failure

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Background: peak oxygen consumption (peak VO_2) is an important prognostic marker in chronic heart failure (CHF) patients. Peak VO_2 reflects oxygen extraction from the metabolically active tissues (i.e., the skeletal muscles); nevertheless, peak VO_2 is expressed in mL/min/kg of body weight (peak VO_2-weight). We assessed, whether the adjustment of peak VO_2 for lean tissue (peak VO_2-lean) might provide better prognostic information than peak VO_2-weight in CHF patients. **Methods**: Prospectively, 272 CHF outpatients in stable clinical conditions (mean age 61±12 years, NYHA class 2.3±0.8) underwent a symptom-limited cardiopulmonary exercise testing, and evaluation of body composition with dual-energy X-ray absorptiometry. **Results:** Peak VO_2-weight averaged 17.6±5.7 mL/kg/min and peak VO_2-lean 25.6±8.1 mL//kg/min. During follow-up (mean 878±777 days), 60 patients died (12-month survival: 89% [95% CI 85-93]). Cox proportional hazard analyses showed that peak VO_2-weight and peak VO_2-lean predicted survival (both p<0.0001), but at the log-likelihood ratio test peak VO_2-lean was significantly stronger than peak VO_2-weight in predicting survival (p=0.002). The receiver operating characteristic area under the curve for peak VO_2-lean was significantly greater than for peak VO_2-weight at 12 , 15, 18 and 21 months follow-up (all p<0.03). In patients with mild CHF, peak VO_2-lean significantly predicted outcome (p=0.03), while peak VO_2-weight lost its prognostic power. **Conclusion:** Adjustment of peak VO_2 for lean tissue instead for body weight provides a stronger prognostic parameter. This correction might be particularly useful in mild CHF and in subgroups of patients, such as in women and obese patients, in whom the prognostic value of peak VO_2 is less obvious.

1086-158 Differential Effects of Carvedilol and Metoprolol on Sympathetic Regulation of Peripheral Vascular Resistance in Patients With Chronic Heart Failure

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Increased vascular resistance in the skeletal muscle circulation of patients with chronic heart failure (CHF) is partly due to activation of the sympathetic nervous system. While the beneficial myocardial effects of inhibition of the sympathetic nervous system with beta-blockade have been previously studied, the effects of pharmacologically distinct beta-blockers on adrenergic regulation of vasomotor tone in patients with CHF are unknown. Accordingly, the current study was undertaken to assess the effect of chronic beta-blocker therapy on peripheral vascular responses to cold pressor test in patients with CHF. We hypothesized that the peripheral vascular effects of carvedilol, an alpha- and non-selective beta-adrenergic receptor antagonist, and metoprolol, a selective beta-adrenergic receptor antagonist would differ.METHODS: Forearm vascular responses to cold pressor test (CPT)(immersion of hand and wrist in ice water for 2 minutes) was determined with strain gauge venous occlusion plethysmography in 26 patients with Class I-III CHF (mean age 55 years, mean EF 27%), treated with ACE-I, digoxin and diuretics. Forearm blood flow (FBF ml/min/100ml) was determined at 15s intervals during supine rest, during CPT and after 5 minutes of arterial occlusion. Mean arterial pressure (MAP, mmHg) was determined in the contralateral arm with an automated cuff method. Forearm vascular resistance (FVR) was calculated in arbitrary units as the ratio of MAP and FBF. FVR was measured before and after 6 months of randomized assignment to carvedilol (25 mg bid, n=15) or metoprolol (ToprolXL 200 mg/day, n=10). RESULTS: In patients treated with carvedilol, FVR during CPT increased by 32.5% at baseline and by 27.5% after 6 months. In patients treated with metoprolol, FVR during CPT before and after 6 months did not change (20.2% vs 20.9%). Minimal vascular resistance after 5 minutes of transient ischemia decreased in patients treated with carvedilol (2.23 vs 2.04) and increased in patients treated with metoprolol (2.17 vs 2.45). CONCLUSIONS: During chronic therapy, mixed alpha/beta-adrenergic receptor blockade with carvedilol reduces forearm vascular resistance to a greater extent than metoprolol.

1086-159 Does a Combined Treatment With Vitamin E and Atorvastatin Improve Endothelial Function and Ejection Fraction in Patients With Heart Failure? A Double Blind Placebo Controlled Study

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Background: Previous studies have shown that endothelial function is compromised in heart failure and coronary artery disease. Treatment with statins or antioxidant vitamins improves endothelial function in patients with atherosclerosis. In this study we assessed the effect of atorvastatin alone or in combination with vitamin E on endothelial function and ejection fraction in patients with heart failure.

Methods: In this double blind placebo controlled study, 47 patients with heart failure (30 males, 17 females) were enrolled. 16 patients received 10mg atorvastatin/day (group A), 13 patients received atorvastatin 10 mg/day plus vitamin E 400IU/day (group B) and 18 other patients received placebo (group C) for 4 weeks. All patients were NYHA II to IV, having an ejection fraction < 40%. Forearm blood flow was measured using venous occlusion strain-gauge plethysmography. Endothelium dependent flow mediated vasodilation (FMD) was expressed as the % change from baseline to maximal flow during reactive hyperemia. Endothelium independent flow (NTR%) was assessed as the % change from baseline to post sublingual nitroglycerin administration flow. Ejection fraction of the left ventricle was estimated with Simpsons method.

Results. Blood pressure, heart rate, basal forearm blood flow, NTR% and body weight were similar before and after the treatment in these three groups. FMD was significantly increased in groups A and B (from 45.14+/-5.4% and 49.0+/-4.3% to 93.04+/-13% and 73.7+/-5.1% respectively, p<0.01 for both) while no significant change was observed in group C. The improvement of FMD was not different between groups A and B. Ejection fraction was also improved in groups A and B (from 26.1+/-0.91% and 23.1+/-0.9% to 28.92+/-1.1% and 27.1+/-1.1% respectively, p<0.05 for both), while remained unaffected in group C (from 25.9+/-0.88% to 26.7+/-1.0%, p=NS).

Conclusions: These findings indicate that atorvastatin treatment for 4 weeks significantly improves endothelial function and ejection fraction in patients with ischemic heart failure. Combined administration of atorvastatin and vitamin E does not offer any further improvement of these two parameters.

1086-160 Coronary Endothelial Dysfunction Occurs Early in the Pathophysiology of Heart Failure

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Background: Though coronary endothelial dysfunction is associated with heart failure, relatively little is known regarding their temporal relationship. We hypothesized that endothelial dysfunction is an early feature of systolic left ventricular dysfunction. The purpose of this study was to evaluate whether coronary endothelial dysfunction is present in patients with aymptomatic left ventricular dysfunction.

Methods: 371 consecutive patients with normal or mild coronary atherosclerosis at angiography underwent assessment of coronary endothelium-dependent vasomotion using intracoronary acetylcholine (ACH), and coronary flow reserve (CFR) was measured with intracoronary adenosine. Coronary blood flow (CBF) was derived from measurements of epicardial diameter (ED) and blood velocity using quantitative angiography and Doppler guidewire, respectively. Patients were divided into two groups: left ventricu-